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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/599,700	02/16/2007	Tobias Mochel	06275-523US1 101400-1P US	2947

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EXAMINER	
CHANDRAKUMAR, NIZAL S	
ART UNIT	**PAPER NUMBER**
1625	

NOTIFICATION DATE	DELIVERY MODE
01/21/2009	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

PATDOCTC@fr.com

Office Action Summary	Application No.	Applicant(s)	
	10/599,700	MOCHEL ET AL.	
	Examiner	Art Unit	
	NIZAL S. CHANDRAKUMAR	1625	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-10 and 13* is/are pending in the application.

4a) Of the above claim(s) *9 and 13* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8, 10* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Applicant on 01/13/2008 indicated that non-final rejection filed 01/13/2009 is not readable because some pages appear to be missing. I view of this, the following will replace non-final rejection office action filed 01/13/2009.

DETAILED ACTION

Attempts were made to contact attorney of applicants John T. Kendall by telephone on 12/18/2008 and again on 12/31/2008 to discuss possibilities of placing the application in condition for allowance. John T. Kendall did not return the calls.

Election/Restrictions

Applicant's election with traverse of Group I, claims 1-8 and 10, drawn to compounds, in the reply filed on 11/26/2008 is acknowledged. The traversal is on the following grounds:

[1] The present application is the U.S. National Stage of International Application No. PCT/SE2005/000495, filed on April 5, 2005. As such, the present application is subject to unity of invention practice in accordance with 37 CFR 1.475 and 1.499 (see MPEP § 1896). See also MPEP 1893.03(d):

> Examiners are reminded that unity of invention **>(not restriction practice pursuant to 37 CFR 1.141 - 1.146)< is applicable in international applications (both Chapter I and II) and in national stage applications submitted under 35 U.S.C. 371.

[2] 37 CFR 1.475 provides as follows (emphasis added):

> a) An international and a national stage application shall relate to one invention only or to a group of inventions so linked as to form a single general inventive concept ("requirement of unity of invention"). **Where a group of inventions is claimed in an application, the requirement of unity of invention shall be fulfilled only when there is a technical relationship among those inventions involving one or more of the same or corresponding special technical features.** The expression "special technical features" shall mean those technical features that define a contribution which each of the claimed inventions, considered as a whole, makes over the prior art.
>
> (b) **An international or a national stage application containing claims to different categories of invention will be considered to have unity of invention if the claims are drawn only to one of the following combinations of categories**:
>
> (1) A product and a process specially adapted for the manufacture of said product; or
>
> (2) A product and process of use of said product; or
>
> **(3) A product, a process specially adapted for the manufacture of the said product, and a use of the said product**; or
>
> (4) A process and an apparatus or means specifically designed for carrying out the said process; or
>
> (5) A product, a process specially adapted for the manufacture of the said product, and an apparatus or means specifically designed for carrying out the said process.
>
> (c) If an application contains claims to more or less than one of the combinations of categories of invention set forth in paragraph (b) of this section, unity of invention might not be present.
>
> (d) If multiple products, processes of manufacture or uses are claimed, the first invention of the category first mentioned in the claims of the application and the first recited invention of each of the other categories related thereto will be considered as the main invention in the claims, see PCT Article 17(3)(a) and § 1.476(c).

(e) The determination whether a group of inventions is so linked as to form a single general inventive concept shall be made without regard to whether the inventions are claimed in separate claims or as alternatives within a single claim.

[3] Presently, the Office is requiring that Applicants elect one of the following groupings of claimed subject matter (Office Action, page 2):

Group I, claim(s) 1-8, 10, drawn to compounds.

Group II, claim(s) 9, drawn to process of making compounds.

Group III, claim(s) 13, drawn to method of treating diseases.

37 CFR § 1.475(b)(3) states that a national stage application containing claims to different categories of invention will be considered to have unity of invention if the claims are drawn to a combination of "[a] product, a process specially adapted for the manufacture of the said product, and a use of the said product" (*supra*). Here, claim 9 is directed to a process for the preparation of a compound of formula (I); and claim 13 is directed to methods of treating a chemokine mediated disease state, which include administering a compound of formula (I). As such, each of claims 9 and 13 shares a special technical feature: the compounds of formula (I), which is also the same special technical feature required by claim 1. Thus, the present claims are drawn to a combination of "[a] product, a process specially adapted for the manufacture of the said product, and a use of the said product." As such, the present claims are unified, and claims 9 and 13 should be rejoined and examined in concert with claims 1-8 and 10 for at least this reason.

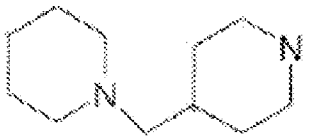
Applicants note that the Office **must** follow PCT Rule 13 and not national practice in these determinations. Thus, even if the Groups were properly restricted under national practice (and Applicants do not concede that to be the case), PCT Rule 13 requires, in this case, rejoinder of the Groups. Thus, all claims, regardless of whether they are compound, method of using, or process of making possess unity in the present case and should be examined in concert in the present application.

This is not found persuasive because for reasons of record.

This application is a 371 of PCT/SE2005/000495 04/05/2005.

The inventions listed as Groups 1-3 do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons: The invariant group in all the groups piperidinylmethylpiperidine is well known in the art. See abstract of applicant provided prior art WO2004/099144 A1.

Thus, common technical feature present in all the groups is



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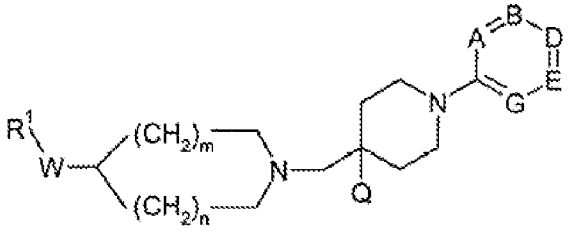
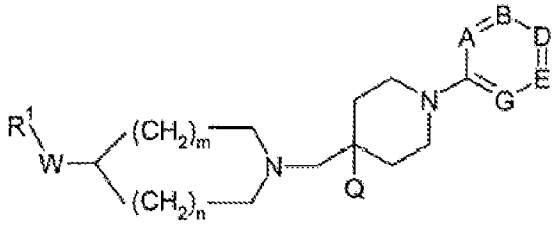
The above structural moiety is taught in the previously cited prior art as follows (see Abstract).



The above formula, when n = 1, corresponds to the instant claim formula



.

As such the invariant present in the three groups of the Restriction Requirement is not a contribution over the prior art. (Also see below for additional prior art citations).

As to applicant's traversal with respect to 'rejoinder issue', the following can be found in the Restriction Requirement papers pages 3 and 4, filed 10/28/2008.

> The examiner has required restriction between product and process claims. Where applicant elects claims directed to the product, and the product claims are subsequently found allowable, withdrawn process claims that depend from or otherwise require all the limitations of the allowable product claim will be considered for rejoinder. All claims directed to a nonelected process invention must require all the limitations of an allowable product claim for that process invention to be rejoined.

In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103 and 112. Until all claims to the elected product are found allowable, an otherwise proper restriction requirement between product claims and process claims may be maintained. Withdrawn process claims that are not commensurate in scope with an allowable product claim will not be rejoined. See MPEP § 821.04(b). Additionally, in order to retain the right to rejoinder in accordance with the above policy, applicant is advised that the process claims should be amended during prosecution to require the limitations of the product claims. Failure to do so may result in a loss of the right to rejoinder. Further, note that the prohibition against double patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01.

The requirement is still deemed proper and is therefore made FINAL.

Claims 9 and 13 withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected inventions, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 11/26/2008.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1 (and by virtue of dependency claims 2-8 and 10) rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The claims are drawn to N-oxides of the formula. There at least 3 nitrogens in the core structure of the claimed formula. It is unclear N-oxide of which nitrogen, applicant is seeking protection for.

Applicant is reminded of *In re Zletz*, 13 USPQ2d 1320, 1322. “An essential

purpose of patent examination is to fashion claims that are precise, clear, correct and unambiguous."

The specification page 5 defines N-oxide as

> An N-oxide of a compound of formula (I) is, for example, a 1-oxy-[1,4']bipiperidinyl-1'-yl compound.

The incomplete nature of the structural definition coupled with lack of working examples of such compounds renders the claim vague.

Deletion of the term N-oxide from the claim would overcome the rejection.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

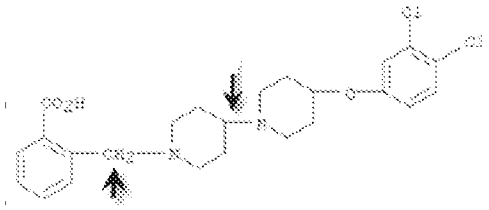
> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

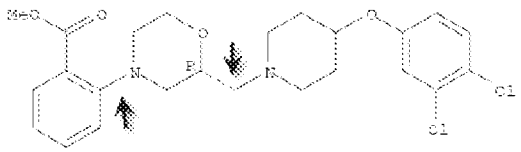
Claims 1-8, 10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Rigby et al. US 6,903,115 (recited on 1449) supplemented with CA135:318419, in view of Luckhurst et al. WO 03/078395 (recited on 1449) supplemented with CA139:276907.

Rigby et al. '115 and Luckhurst et al. '395 are analogous are on CCR3 binding compounds. An example disclose by Rigby et al. has very similar structure as the claims



See delineation by CA135.

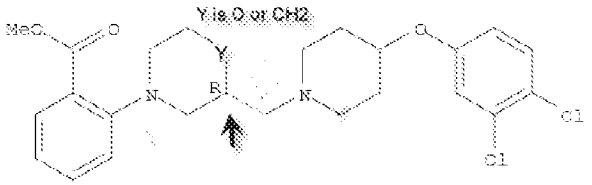
The difference between the prior art compound and the instant claims is the insertion of one methylene linker between the two piperidine rings (see mark supra) and the omitting of one methylene linker between the Ar and the piperidine ring. Luckhurst et al. '395 taught that insertion of a methylene linker is an optional choice for such compounds:



One having ordinary skill in the art is deemed to be aware of all the pertinent art in the field. The possession of the above compounds and the generic teaching of the references would motivated one to modify one proven compound with another proven compound with the attributes described and exemplified by the references. Not only the generic teaching of the prior art clearly indicated that insertion of methylene linker between rings would not affect activity, one in the chemical art would expect the switched methylene chain compounds would have similar configuration thus would expect such modification to render compounds with expected activity.

Claims 1-8, 10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Luckhurst et al. WO 03/078395 (recited on 1449) supplemented with CA139:276907 in view of Rigby et al. US 6,903,115 (recited on 1449) supplemented with CA135:318419.

Luckhurst et al. '395 disclosed structurally close compounds as the claims:



The difference between the Luckhurst et al. '395 compounds and the instant claims is the position isomerism of the 3-substitution and the instantly claimed 4-

position. Not only position isomerism has long been recognized in the medicinal compound art to be prima facie obvious modification (see Ex parte Engelhardt 208 USPQ 343; In re Mehta 146 USPQ 284), but also, it is taught in the analogous art by Rigby et al. '115, that the attachment of the two piperidinyl rings can be at variable positions.

One having ordinary skill in the art in possession of the above reference would be motivated to modify the Luckhurst et al. '395 compounds with the positional variation with the expectation that position isomerism is a tool to obtain more useful compounds and the expectation that the modified compounds would have compatible activity such as recognized in the analogous art.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29

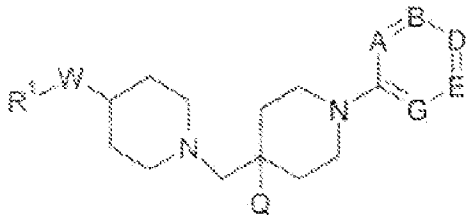
USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

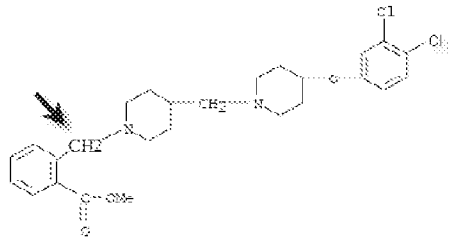
Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-8, 10 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over the pending claims of copending Application No. 10/528,477 in view of WO03/078395.

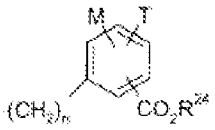
The instant claims are drawn to the following formula:



SN 10/528,477 is claiming the compounds such as:



The insertion of one methylene chain was taught by WO03/078395 wherein the substituent on the piperidine nitrogen Z is:

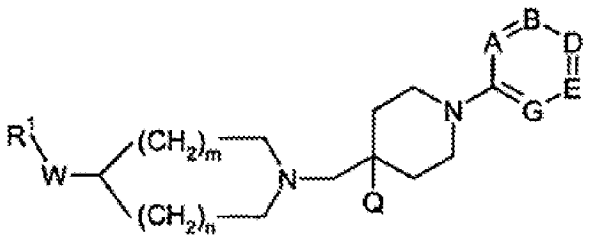


Wherein n=0 or 1, i.e. direct attached like the instant claims; or one methylene inserted as the copending claims.

The insertion of one methylene is a prima facie obvious structural modification and decisions on such findings are well set forth by the court. See In re Ruddy 121 USPQ 427; Ex parte Gresham 121 USPQ 422; Ex parte Nathan 121 USPQ 349.

Claims 1-8, 10 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over the pending claims of copending Application No. 10/556107.

Claims of '107 are drawn to compounds of formula



when n = 1, the formula is the same as the formula of the instant claims. Further, the alleged usefulness of the instantly compounds and the compounds of the copending application are the same.

This is a provisional obviousness-type double patenting rejection.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-8 and 10 rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for *making* some compounds of the claims does not reasonably provide enablement for *using* compounds of the claims. For example, it is not seen where in the specification enabling disclosure is found for making N-oxides of the claimed formula (I). The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The following eight different factors (see Ex parte Foreman, 230 USPQ at 547; Wands, In re, 858.F. 2d 731, 8 USPQ 2d 1400, Fed. Cir. 1988) must be considered in order for the specification to be enabling for what is being claimed:
Quantity of experimentation necessary, the amount of direction or guidance provided, presence or absence of working examples, the nature of the invention, the state of the prior art, the relative skill of those in the art, the predictability or unpredictability and the breadth of claims. In the instant case, the specification is not enabling based on at least four of the above mentioned eight different factors such as quantity of experimentation necessary, the amount of direction or guidance provided, presence of working examples, state of the prior art, unpredictability and the breadth of claims.

The enabling disclosure with respect to making aspect of the enablement requirement is limited. For example, while direction and guidance are present for making compounds of formula (I) wherein Q is H is found in the specification, there is only a speculative method disclosed for making compounds wherein Q is OH (see page 8 last lines). There are no working examples of such compounds. Likewise, barring the vague definition (see rejection under 112-2) of N-oxides there is no disclosure with respect to how make and use N-oxides of the compounds of the formula (I). There is no teaching in the specification (by way of direction, guidance or working examples) or by prior art citation, how to obtain regio-selectively, N-oxides. Therefore, in absence of teachings, guidance, presence of working examples and unpredictability, it would require undue experimentation to make the compounds of the invention.

With respect to use aspect of the enablement requirement, the specification teaches that the instant compounds are antagonists of chemokine CCR3 receptor and histamine H1 receptor in vitro and also have binding affinity for histamine H1 receptor. There is no teaching or guidance presents in the specification or prior art that hyperactivity of CCR3 receptors or H1 receptors is implicated in the etiology of every known disease condition mediated by activation of all the different receptor subtypes of chemokines . There is no teaching in the prior art that structurally closely related compounds having antagonist activity at CCR3 receptors or H1 receptors are well known to have therapeutic utility in treating every known disease condition mediated by activation of all the different receptor subtypes of chemokines. There is no working examples present showing efficacy of instant compounds in known animal models of

any disease condition which is mediated by chemokines. The instant compounds of formula (I) encompasses hundreds of thousands of compounds based on the numerous variables layered on top of variables and therefore, in absence of such teachings, guidance, presence of working examples and prior art, it would require undue experimentation to demonstrate efficacy of instant compounds in known animal models of every known disease condition which is mediated by chemokines and hence their utility for treating these disorders.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to NIZAL S. CHANDRAKUMAR whose telephone number is (571)272-6202. The examiner can normally be reached on 8.30 AM - 4.30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet Andres can be reached on 571 0272-0867. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Nizal S. Chandrakumar

/D. Margaret Seaman/

Primary Examiner, Art Unit 1625